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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,184	12/06/2001	E. Scott Priestley	PH-7087-A	8535
23914	7590	06/10/2004	EXAMINER	
STEPHEN B. DAVIS BRISTOL-MYERS SQUIBB COMPANY PATENT DEPARTMENT P O BOX 4000 PRINCETON, NJ 08543-4000			LUKTON, DAVID	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/010,184

Applicant(s)

PRIESTLEY ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-8 is/are allowed.
- 6) ☒ Claim(s) 9-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Applicants' election of Group I is acknowledged, as is the elected specie. Claims 18-26 are now rejoined with the elected claims.



The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification asserts (page 101, line 27+) that "a number of compounds" exhibit a K_i below 60 *micromolar*. It is stipulated at this point that HCV NS3 protease can be inhibited both *in vitro* and *in vivo*. It is further stipulated that the compounds will inhibit replication of hepatitis C virus in a mammal. However, it does not follow therefrom that the specification enables the skilled virologist to use the compounds to treat a hepatitis C infection in a mammal. It is not established that the NS3 protease will be inhibited to an extent which is sufficient to actually cause a reduction in viral titers. For example, if the virus is replicating at a rate of 100 "units" per day in the absence of the compound, and 90

units per day in the presence of the compound, one could say that inhibition had been achieved. However, if the virus is replicating at a rate of 90 per day in spite of the presence of the compound (of claim 1), the patient's condition will still worsen, and "treatment" will not have been achieved.

Claims 9-17 are rejected for each of two separate reasons: (a) each of these claims recites the term "pharmaceutical", which implies an assertion of therapeutic efficacy, and (b) each of these claims recites the term "therapeutically effective". Claims 18-25 are rejected, not because they are drawn to a method of inhibiting HCV NS3 protease, but because each of these claims recites the phrase "therapeutically effective".

As stated in *Ex parte Forman* (230 USPQ 546, 1986) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

As it happens, structure/activity relationships are unpredictable. As observed by Tung (WO 98/17679), compounds within that disclosed genus (table 9, pp. 106-107) exhibited more than a 100-fold range of efficacies in the inhibition of HCV NS3 protease. Many of those compounds characterized as exhibiting an inhibition above 100 *micromolar* may have been completely inactive. (See also table I of WO 99/07734). Accordingly, the skilled

artisan would conclude that, where antiviral compounds are concerned, structure/ activity relationships (*in vitro*) are unpredictable. Therapeutic efficacy is similarly unpredictable. As for the "state of the art", there is no evidence that anyone has effectively treated an HCV infection in a mammal using an inhibitor of HCV NS3 protease. Moreover, as stated in Ingallinella (*Biochem.* 37, 8906, 1998) at page 8906, col 1:

"Neither an effective therapy for HVC nor a vaccine... has ... been developed".

In accordance with the following, "undue experimentation" would be required to practice the claimed invention. It is suggested that (a) the term "pharmaceutical" be deleted from each claim which recites it, (b) the term "therapeutically effective amount" be deleted at every occurrence, and (c) that claim 26 be cancelled.

✱

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



DAVID LUKTON
PATENT EXAMINER
GROUP 1653